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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| STRZELECKA, TERESA E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/067,543 | BYRD ET AL. | |
| | Examiner | Art Unit | |
| | Teresa E Strzelecka | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-6,13-16,34,35,54,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,13-16,34,35,54,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/7/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. This office action is in response to an amendment filed July 27, 2004. Claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 were previously pending. Applicants amended claims 1, 13, 54, 58 and 59. Claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 are pending and will be examined.

2. Applicants' amendments overcame the following rejections: rejection of claims 16 and 58 under 35 U.S.C. 112, second paragraph; rejection of claim 54 under 35 U.S.C. 102(b) as anticipated by Pace et al. All other rejections are maintained for reasons given in the "Response to Arguments" section below.

### *Information Disclosure Statement*

3. The information disclosure statement (IDS) submitted on September 7, 2004 was filed after the mailing date of the non-final rejection on January 27, 2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### *Response to Arguments*

4. Applicant's arguments filed July 27, 2004 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 under 35 U.S.C. 112, first paragraph, written description, Applicants argue that:

a) one of ordinary skill in the art would readily understand the term "recombination site" and, therefore, would conclude that Applicants were in possession of the claimed invention,

b) the specification provides a number of representative examples of the claimed genus of Ter-sites, therefore, the representative number of the genus is described in the specification.

B) Regarding the rejection of claims 1, 3-6, 34, 58 and 59 under 35 U.S.C. 102(b) as anticipated by Lee et al., Applicants argue that Lee et al. do not anticipate all of the elements of claim 1, since they do not teach recombination sites such as att, lox, etc.

C) Regarding the rejection of claims 13 and 14 under 35 U.S.C. 103(a) over Neylon et al. as evidenced by Jonsson et al., Applicants argue that Neylon et al. do not teach recombination sites or a solid support comprising at least one oligonucleotide comprising a Ter-site.

D) Regarding the rejection of claims 15 and 16 under 35 U.S.C. 103(a) over Neylon et al. and Gold et al., Applicants argue that since Neylon et al. do not disclose limitations of claim 13, so Neylon et al. and Gold et al. do no not suggest claims 15 and 16.

With respect to A), Apllicants cite examples of 25 Ter sites from different organisms on pages 22 and 23 of the specification. However, on page 21, in paragraph [0074], Applicants provide the following description:

"Ter-sites according to the invention are any replication termination sequence from any source including those found in eukaryotic and prokaryotic (including gram positive and gram negative microorganisms). The invention also contemplates any portion of such Ter-sites that may be recognized and bound by one or more Ter-binding proteins such as replication terminator proteins or peptides."

Therefore, Applicants contemplate hundreds of thousands if not millions of possible sequences, since the only requirement for a site to be a Ter-site is to be any replication termination sequence or its fragment. From this point of view presentation of 25 exemplary Ter-sites, which do not have any common sequence motifs, hardly amounts to providing a representative number of species of this extremely large genus.

In terms of recombination sites, as Applicants are well aware, any sequence can serve as a recombination site, as long as it is complementary to a sequence in the target nucleic acid molecule, therefore, since the "recombination site" can be any sequence and Applicants have not defined or described any recombination sites, Applicants have not provided a representative number of species in the claimed genus.

The rejection is maintained.

With respect to B), Applicants did not define what a termination site is, and, in addition, any sequence can serve as a recombination site, therefore, since Lee et al. teach plasmids containing Ter-binding sites and other nucleic acid sequences, they also teach recombination sequences.

With respect to C), since Applicants did not define what a "recombination site" is, this term can be interpreted as any nucleic acid sequence. Therefore, Neylon et al. anticipate claims 13 and 14. Further, Neylon et al. teach a solid support in a form of a BIACORE chip, therefore, they anticipate claims 13 and 14.

With respect to D), arguments regarding the Neylon et al. reference were addressed above, therefore, the combination of Gold et al. and Neylon et al. makes claims 15 and 16 obvious.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID NO: 1-25. No sequences were provided for the recombination sites. Thus, applicant has express possession of only twenty five particular Ter sites, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences, which meet these functional limitations, is provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the

> patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the Ter-binding sites lack any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the twenty five specific sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "an isolated nucleic acid molecule comprising at least one binding site for a Ter-binding protein", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a Ter-binding site, without any definition of the particular site claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise Ter-binding sites represented by SEQ ID NO: 1-25. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 3-6, 34, 58 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (J. Biol. Chem., vol. 267, pp. 8778-8784, 1992) and evidenced by Bussiere et al. (Mol. Microbiol., vol. 31, pp. 1611-1618; cited in the IDS).

Regarding claims 1 and 58, Lee et al. teach an isolated nucleic acid molecule engineered to comprise two Ter-sites (plasmid oriC-terCW.CCW). The nucleic acid comprises an origin of replication. The Ter sites are arranged with respect to the origin of replication in such a way that the sequence between the Ter sites which does not contain the origin of replication is not replicated in cells expressing a replication termination protein (Fig. 1 (c); Fig. 2, 3).

Regarding claim 3, Lee et al. teach TerB sites (Fig. 1 (c)).

Regarding claim 4, Lee et al. teach plasmids (Fig. 1 (c)).

Regarding claim 5, Lee et al. teach a linear molecule comprising the Ter sites capable of being bound by a Ter-binding protein (Fig. 4 (a)).

Regarding claim 6, Lee et al. teach plasmids comprising restriction enzyme recognition sequences (Fig. 1 (c)).

Regarding claim 34, Lee et al. teach composition comprising plasmid oriC-terCW.CCW and Ter-binding protein (page 8778, the last paragraph, continued on page 8779; Fig. 3).

Regarding claims 35 and 59, Lee et al. teach ter-binding protein (TBP) from *E. coli* (page 8779, first full paragraph). Lee et al. do not use the term "Tus" for this protein. Bussiere et al. teach that the ter-binding protein of *E. coli* is Tus (page 1615, fourth paragraph). Therefore, Lee et al. teach Tus protein.

9. Claims 13 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Neylon et al. (Biochemistry, vol. 39, pp. 11989-11999, October 2000; cited in the IDS) as evidenced by Jonsson et al. (Biotechniques, vol. 11, pp. 620-627, 1991).

Regarding claims 13 and 14, Neylon et al. teach a solid support (BIACORE chip) comprising oligonucleotides comprising Ter sites (page 11990, second paragraph; Table 2). Neylon et al. do not specifically teach that the solid support is a non-biological material. However, as evidenced by Jonsson et al., the BIACORE chip consists of glass support coated with gold film, therefore the solid support a non-biological material.

10. Claim 54 is rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene Catalog (page 17, 1992), as evidenced by Short et al. (Nucleic acids Res., vol. 16, pp. 7583-7600, 1988).

The Stratagene Catalog teaches a kit comprising Lambda ZAP vector (= isolated DNA molecule), host strain, helper pages R408 and VCSM13 (page 17). As evidenced by Short et al., the vector contains terminator sequences (page 7584, third paragraph), therefore, the Stratagene Catalog teaches an isolated DNA molecule comprising at least one Ter site, and, since Applicants did not define the term "recombination sequence", it also teaches recombination sequences. Further, since the kit contains host cells for the plasmid, which are E. coli cells (Short et al., page 7585, second paragraph), which inherently contain Ter-proteins, DNA polymerases and recombination proteins, the Stratagene Catalog anticipates all of the limitations of claim 54.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neylon et al. and Gold et al. (U.S. Patent No. 6,242,246).

A) Claim 15 is drawn to a solid support of claim 13 wherein the oligonucleotide is capable of forming a stem-loop or hairpin, and claim 16 is drawn to a solid support of claim 15, where a duplex portion of the stem-loop or hairpin comprises a Ter-site.

B) Neylon et al. teaches an assay which includes binding of Tus to double-stranded Ter sites, but also to single stranded DNA and non-specific sequences. Neylon et al. do not teach oligonucleotides capable of forming stem-loop or hairpin or oligonucleotides with the Ter-sites in the duplex portion of the stem-loop or hairpin.

C) Gold et al. teach solid support with stem-loop nucleic acid molecules which can bind target molecules, such as proteins (col. 4, lines 33-36; Fig. 6; col. 14, lines 26-67;

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the hairpin nucleic acids of Gold et al. in the assays of Neylon et al. The motivation to do so would have been that using hairpin nucleic acids allowed detection of binding to single-stranded (loop of the stem-loop or hairpin) and double-stranded (stem of the stem-loop or hairpin) nucleic acids utilizing single nucleic acid molecules.

13. No claims are allowed.

***Conclusion***

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
10/12/2004

JEFFREY FREDMAN
PRIMARY EXAMINER
10/14/04